

to disclose; **S. Kolvekar**: Nothing to disclose; **J. Tsui**: Nothing to disclose; **R. Yu**: Nothing to disclose.

#### PS186.

##### **Efficacy of Antibiotic-Impregnated Bone Cement Beads Against Organisms Found in Abdominal Vascular Graft Infections**

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**Objectives:** Graft infection often involves several different organisms. Antibiotic-impregnated polymethyl-methacrylate (PMMA) beads may be effective in controlling reinfection after infected graft replacement. We sought to determine an effective antibiotic combination in PMMA beads for use in vascular graft infection.

**Methods:** PMMA beads were impregnated with different combinations of antibiotics including daptomycin (DA), tobramycin (TO), and meropenem (ME). Beads were plated into separate 0.8% Mueller-Hinton agar plates with vancomycin-resistant enterococcus (VRE), *Klebsiella*, *S. epidermidis*, and methicillin-resistant *Staphylococcus aureus* (MRSA). Antibiotic inhibition was recorded in millimeters using the disc agar-diffusion method and averaged from three separate platings.

**Results:** DA alone was not active against *Klebsiella* (average = 0 mm). TO alone was not active against VRE, *Klebsiella*, or MRSA. ME showed broad-spectrum activity against all organisms with >15 mm inhibition halo. The efficacy of ME was decreased by TO but not DA. Adding DA and TO to ME did not improve efficacy.

**Conclusions:** Meropenem in PMMA beads shows activity against difficult pathogens encountered in vascular graft infections. Daptomycin can be added for double-coverage against multi-drug resistant gram-positive pathogens such as VRE and MRSA. Tobramycin appears to reduce the efficacy of meropenem when used in combination.

**Author Disclosures:** **A. Azizzadeh**: Nothing to disclose; **K. M. Charlton-Ouw**: Nothing to disclose; **F. Kubrusly**: Nothing to disclose; **S. S. Leake**: Nothing to disclose; **H. J. Safi**: Nothing to disclose; **H. K. Sandhu**: Nothing to disclose.

**Table.** Average inhibition halo in millimeters

	VRE	<i>Klebsiella</i>	<i>S. epidermidis</i>	MRSA
DA	9.8	0	10.2	9.6
TO	2.0	10.7	14.0	4.7
DA + TO	8.0	10.8	14.3	9.9
ME	17.0	15.3	21.0	17.3
ME + DA	17.2	16	21.7	17.7
ME + TO	13.8	13.5	16.7	13.4
ME + DA + TO	16.9	15.0	21.0	17.0
Control	3.2	6.9	8.7	4.2

#### PS188.

##### **Is Oxidative Stress Important in AAA Pathogenesis?**

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**Objectives:** Active investigations continue to identify markers other than size that would predict a risk of AAA rupture. Circulating biomarkers could also indicate optimal intervals between the surveillance intervals. Finally, the identification of biomarkers also may identify potential pathogenic pathways, and thus may open possibilities for pharmacological inhibition of growth. In the search of novel biomarkers of AAA progression, serum and wall material proteins were analyzed by a differential proteomic approach.

**Methods:** Same layers of AAA wall from ruptured (rAAA) and non-ruptured AAA were incubated, and the proteins released were analyzed by 2-dimensional difference in-gel electrophoresis. Proteins from serum were analyzed and correlated with AAA annual expansion rate.

**Results:** Several differentially expressed proteins involved in main AAA pathological mechanisms (proteolysis, oxidative stress, and thrombosis) were identified by mass spectrometry. Among the proteins identified, peroxiredoxin-2 (PRX-2) was more permanent, which was further validated by Western blot and immunohistochemistry. We demonstrated increased PRX-2 serum levels in rAAA patient wall material compared with AAA subjects and also positive correlation in serum among PRX-2 and AAA diameter and annual expansion rate. Finally, a prospective study revealed a positive correlation between PRX-2 serum levels and AAA expansion rate.

**Conclusions:** Several proteins associated with AAA pathogenesis have been identified by a proteomic approach. Protein profiles identified in the serum would appear to be a convenient monitoring tool that has the ability to be both sensitive and specific for AAAs. PRX-2 serum levels are increased in rAAA patients and correlate with AAA size and growth rate, suggesting the potential use of PRX-2 as a biomarker for AAA evolution.

**Author Disclosures:** **J. Sander mann**: Nothing to disclose; **G. Urbonaviciene**: Nothing to disclose; **S. Urbonavicius**: Nothing to disclose.

#### PS190.

##### **Urine mRNA as an Early and Novel Marker of Contrast-Induced Kidney Injury (CIKI)**

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**Objectives:** CIKI is a common etiology of renal dysfunction in hospitalized patients, and affects the daily practice of vascular surgeons. It increases mortality, costs and LOS; yet no direct or specific marker exists. Indirect

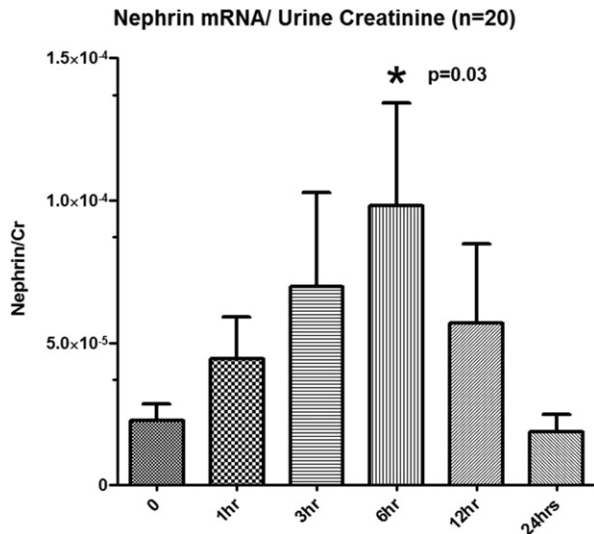
elevations of serum creatinine occur days later and research into makers of early kidney injury has focused on various proteins with disappointing results. Our animal data revealed that even low dose contrast leads to kidney injury and nephron-specific mRNA can be detected in the urine. We wished to evaluate if nephron-specific mRNA could be detected in patients after endovascular procedures as a new, specific marker for CIKI.

**Methods:** Adults undergoing endovascular procedures requiring contrast were consented. Urine was collected over 24hrs. Urinalysis and mRNA extraction followed. rtPCR using nephron-specific (Nephrin, Podocin, Aquaporin-2) and a non-specific (TBF-Beta) probes. Clinical data was also collected.

**Results:** Avg contrast:116cc. Avg age:69. Significant increases were found only in Nephrin mRNA at 6hrs, and returned to baseline (n = 20;  $P = .03$  - see graph). Hematuria preceded this at 3hrs ( $P < .02$ ) after contrast exposure. There was no increase in the serum Cr (it decreased).

**Conclusions:** Consistent with our animal model, Nephrin mRNA and blood are detectable in the urine within hours after contrast exposure, regardless of serum creatinine. Urine mRNA is a potentially sensitive marker for CIN.

**Author Disclosures:** S. Blackburn: Nothing to disclose; A. Borisov: Nothing to disclose; G. A. Escobar: Nothing to disclose; T. Gangal: Nothing to disclose; R. Patel: Nothing to disclose; D. Slack: Nothing to disclose.



**Fig.** Nephrin mRNA detected in urine (normalized to urine creatinine) prior to contrast exposure (time 0) or up to 24 hours after first contrast dose.

## PS192.

### Inhibition of Hypoxia Inducible Factor (HIF)-1 $\alpha$ Suppresses Formation and Progression of Experimental Abdominal Aortic Aneurysms (AAAs)

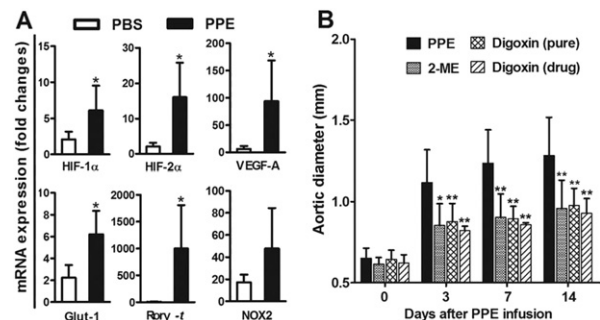
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**Objectives:** HIF-1 $\alpha$  critically regulates angiogenesis, a histopathological feature of AAA disease. This study evaluated whether 2-methoxyestradiol (2-ME) or digoxin, known HIF-1 $\alpha$  inhibitors, modulate experimental AAAs.

**Methods:** AAAs were created in male C57BL/6J mice via transient intra-aortic porcine pancreatic elastase (PPE) infusion. Mice were treated with vehicle, 2-ME (50 mg/kg/day) or digoxin (2 mg/kg/day) starting prior to, or following, PPE infusion. Therapeutic efficacy was evaluated using serial aortic diameter ultrasound imaging and histological analyses at sacrifice.

**Results:** mRNAs for HIF-1 $\alpha$  and four genes regulated by HIF-1 $\alpha$ , were up-regulated in aneurysmal aortae. In vehicle-treated mice, aortic diameters enlarged remarkably and persistently beginning the third day following PPE infusion. Pretreatment with either 2-ME, or digoxin, significantly attenuated subsequent PPE-induced aortic expansion (Fig). Initiated 4 days following PPE infusion, treatment with both drugs also prevented further enlargement of existing AAAs. Histologically, treatment with 2-ME or digoxin was associated with preserved medial smooth muscle cellularity and elastic fibers, and reduced mural leukocyte infiltration and angiogenesis.

**Conclusions:** Pharmacological inhibition of HIF-1 $\alpha$  suppresses formation and progression of PPE-induced AAAs, suggesting the translational potential for HIF-1 $\alpha$  inhibition in human AAA therapy.



**Fig.** HIF-1 $\alpha$  inhibition suppresses experimental AAA. Male C57BL/6J mice were treated with vehicle, 2-ME (50 mg/kg/day) or digoxin (2 mg/kg/day) starting 1 days prior to PRE infusion, for a total of 15 days. Serial aortic diameter measurements were performed using transabdominal ultrasonography. **A**, Fold changes in mRNA expression in HIF-1 $\alpha$  and VEGF-A, Rbry-t, Glut-1, and NOX2 in aneurysmal aortae (PRE infusion) and control aortae (PBS infusion) as compared to normal mouse aortae. **B**, Aortic diameter change following PPE infusion and treatment with vehicle alone, 2ME or digoxin (chemical and pharmaceutical grade) in vehicle. Data presented as mean plus standard deviation. Two-way ANOVA followed by Newman-Keuls test, \* $P < .05$  and \*\* $P < .01$  compared to vehicle treatment. n = 5-8 mice in each group.